UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,963	02/18/2005	David William Tonge	100815-1P US	3567

44992 7590 02/16/2010
ASTRAZENECA R&D BOSTON
35 GATEHOUSE DRIVE
WALTHAM, MA 02451-1215

EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
02/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/524,963	TONGE ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 January 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *26-28,41-43 and 51-53*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). 19 January 2010

13. ☐ Other: _____.

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant again submits lengthy remarks stating that the prosecution of related applications in foreign jurisdictions should provide a reasonably persuasive position to the US Examiner to reconsider the instant patent claims as evidence of patentability. This is, and will continue to remain, unpersuasive. A determination of patentability made by a foreign patent office is not binding on the USPTO. MPEP §901.05 (III) refers to the need to obtain a "separate patent" in "each country in which patent rights are desired," confirming the notion that U.S. patent examination is a process distinct from those of foreign patent offices. Different patent offices use vastly divergent standards of patentability, so a finding that a claim is patentable in one country is not necessarily probative of patentability in another. Findings of foreign patent offices do not obviate Applicant's burden to comply with the relevant patent statutes of the United States. Continued reliance upon this argument as being pertinent to patentability will continue to be unimpressive in establishing that the instant claims circumscribe patentable subject matter. Applicant is urged to address the facts in the case to establish how the instant claims distinguish from the instantly cited prior art and to decline from relying upon the determinations of other foreign jurisdictions to allege patentability of the claims.

Applicant traverses the instant rejection under 35 USC 103(a), stating that one of ordinary skill in the art would not have looked to Bradbury et al. because the reference was one of a number of references directed to ET-1 antagonists at the time of the invention and Bradbury et al. is directed to the treatment of a variety of diseases, which Applicant characterizes as "tangentially" disclosing the treatment of cancers, and further alleges that the selection of this reference to teach the instantly claimed compound was made using impermissible hindsight reconstruction. Applicant provides an ambiguous argument at p.6 of the remarks, stating that "Although the Examiner has suggested that the alternative embodiments by their mere recitation in Bradbury et al. provide support for selection of the particular example (i.e., Compound (I)), this is not true if this reference were the secondary reference to which the ordinarily skilled artisan would be motivated to consult/combine with the disclosure of the primary reference solely to provide a portion of the missing solution to the problem presented, which in this case would be the very compound itself." Applicant again urges the consideration of his submission of secondary considerations, stating that the Examiner has ignored these secondary considerations, which is not permissible in accordance with MPEP 2145. Applicant urges that the specificity of the compound at the ETA receptor (without measurable ETB activity) could not have been predicted by the art and, thus, it would not have been predicted that Compound (I) would have been a suitable agent for treating prostate cancer. Applicant insists that this ETA specificity with lack of measurable ETB activity of the instant compound is unexpected and relies upon the Astrasentan clinical trials as supporting the conclusion that a compound that lacks endothelin-B receptor activity improves the agent's anti-cancer efficacy by not blocking synergistic pro-apoptotic pathways.

Firstly, Applicant is reminded that the volume of prior art at the time of the invention related to ET-1 antagonists is irrelevant. The fact that other artisans were studying ET-1 antagonists at the time of the invention and publishing documents and references related to such a topic does not weigh against the selection of Bradbury et al. as prior art. It remains that Bradbury et al. teaches heterocyclic compounds that function as endothelin-1 (ET-1) antagonists, including the specifically named compound N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadizol-2-yl]phenyl)pyridine-3-sulphonamide, and are useful for treating diseases in which elevated or abnormal levels of endothelin play a significant causative role, including certain cancers. In addition, Applicant's attempt to characterize Bradbury et al. as only "tangentially" disclosing the treatment of cancers is an objectionable characterization of the reference. This is an attempt to diminish the teachings of Bradbury et al. by imputing a hierarchy of importance to the list of diseases disclosed as being treatable using the ET-1 antagonists of the reference that was clearly not set forth by the patentee himself. Applicant then attempts to use this improper characterization of Bradbury et al. to allege that the Examiner's selection of Bradbury et al. was made using impermissible hindsight reconstruction because it is not really "in the sea of cancer art" (p.5, Remarks). The basis of this argument is not understood and directly contradicts the factual teachings of the reference. The instant rejection is very clearly based upon the knowledge and motivation that was generally and publicly available to one of ordinary skill in the art at the time of the invention and does NOT rely upon Applicant's disclosure to formulate the rejection. In addition, the rejection only takes into account the knowledge that was within the level of ordinary skill at the time the claimed invention was made and does not include ANY knowledge that was gleaned only from Applicant's disclosure in order to set forth the instant rejection. Accordingly, this argument is unimpressive. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Secondly, Applicant states, "Although the Examiner has suggested that the alternative embodiments by their mere recitation in Bradbury et al. provide support for selection of the particular example (i.e., Compound (I)), this is not true if this reference were the secondary reference to which the ordinarily skilled artisan would be motivated to consult/combine with the disclosure of the primary reference solely to provide a portion of the missing solution to the problem presented, which in this case would be the very compound itself." This argument is not understood. Bradbury et al. is used as the primary reference in the rejection and very clearly teaches the exact compound as instantly claimed. Applicant's suggestion to hypothetically use it as the secondary reference is irrelevant because this was not how the rejection was set forth. Applicant is again urged to direct his remarks to the facts in the case, not to what may result if the rejection were based upon a different combination or order of references.

Thirdly, Applicant opines that the Examiner has ignored his submission of secondary considerations. This is not a point well taken because it very clearly ignores the discussion dedicated to this issue at p.6-8 of the previous Office Action. Note that the fact that alleged evidence of secondary considerations may be found unpersuasive is NOT the same as choosing to not consider the evidence. Applicant appears to have confused these two possibilities. Applicant cites to MPEP 2145 in support of his position that the Office is required to consider evidence of secondary considerations, but chooses to omit the fact that evidence pertaining to secondary considerations does not necessarily control the obviousness conclusion. This is found in MPEP 2145 and specifically states that, in certain cases, unexpected results may be insufficient to overcome a conclusion of obviousness when the evidence provides such a strong case of obviousness. It is maintained that these alleged "secondary considerations" were already addressed in the prior Office Action, but were found to be unpersuasive.

Nevertheless, such considerations are summarily addressed again infra. Applicant alleges that it was unexpected that the specificity of the claimed compound at the ETA receptor (without measurable ETB activity) would not have been predicted by the prior art and, as a result, would not have suggested that the claimed compound would have been suitable for treating prostate cancer. Applicant relies upon a reference from Nature Reviews Urology (6(350), July 2009) is support of his position that selective antagonists of endothelin A (such as ZD4054) were found to improve overall survival in hormone-resistant metastatic prostate cancer purportedly due to the lack of activity at the endothelin B receptor. Applicant urges that this reference also discusses results of another endothelin antagonist (Astrasentan), which was found to lack efficacy in improving overall survival in prostate cancer progression purportedly because it inhibits signalling mediated by the endothelin B receptor. This is unpersuasive for several reasons: (1) the reference that Applicant cites in support of his position is post-filing date art and fails to establish that this selectivity for endothelin A receptors was a desirable property of an anti-cancer agent at the time of the instant invention. This is unpersuasive because 35 U.S.C. 103(a) clearly stipulates that "a patent may not be obtained…if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." In particular, Applicant's insistence that this could not have been predicted and would have been unexpected by the prior art is immaterial because the prior art at the time of the invention had no recognition or knowledge of the fact that the compound should be selective for ETA and lack ETB activity; and (2) Applicant has failed to show that the claimed compound has any unexpected activity at either ETA and/or ETB that would not have been found in the general class of ET-1 antagonists of Bradbury et al. such that the activity of this one instantly claimed compound had an unexpectedly greater effect than what would have been reasonably expected from the disclosure of the prior art. The mere characterization of a specific property (in this case, the ETA versus ETB activity) of an old compound that was already known in the prior art does not make it newly patentable to Applicant. In other words, Applicant has provided no evidence to support the assertion that the instantly claimed compound distinguishes over any of the other compounds contained in the prior art such that the activity seen with this one single compound would have been sufficiently unexpected such that it mandated a conclusion of nonobviousness. For these reasons, Applicant's urged "secondary considerations" are again found unpersuasive and do not outweigh the evidence provided in support of obviousness.

Lastly, Applicant requests that the provisional obviousness-type double patenting rejections over copending U.S. Patent Application Nos. 11/720,001 and 12/483,821 be held in abeyance. In the absence of any remarks to the contrary, these rejections are maintained. Note, however, that Applicant's request for abeyance is technically not a response in compliance with the provisions of 37 C.F.R. 1.111, which stipulates that requests for abeyance may only be made with regard to formal matters (i.e., not rejections). However, in the interest of compact prosecution, and further given that the instant application is after-final, the response is not held to be non-compliant with the requirements of 37 C.F.R. 1.111. However, Applicant is reminded that requests for abeyance in response to rejections does not comply with the requirements of 37 C.F.R. 1.111 and may be considered non-compliant if provided in future submissions.

For these reasons supra, and those previously made of record at p.2-15 of the final rejection dated November 17, 2009, the claims remain rejected for the reasons of record, which are herein incorporated by reference.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614